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Synthesis of tetrahydro-5-azaindoles and 5-azaindoles using Pictet–Spengler reaction—appreciable difference in products using different acid catalysts

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ABSTRACT

Pictet–Spengler condensation of 2-(aryl)-2-(1*H*-pyrrol-2-yl)ethanamines using conventional acid catalysts like TMSCl or TFA resulted in the formation of substituted 5-azaindoles involving a tandem one pot four steps reaction sequence. By contrast use of glacial acetic acid furnished the targeted tetrahydro-5-azaindoles in diastereoselective manner. These were readily dehydrogenated to 5-azaindoles.

1. Introduction

The interests in azaindoles originated primarily from their medicinal relevance and applications in material synthesis and coordination chemistry. They are frequently exploited as indole bioisosteres in the design of biologically interesting molecules.[1] Many of these compounds show diverse biological activities, such as anti-inflammatory,[2] anti-psychotic,[3] thrombin inhibitor,[4] and fVIIa.TF inhibitor[5] activity. Tetrahydropyrrolo[3,2-*c*]pyridine derivatives are known as inhibitors of ADP-stimulated platelet aggregation in vitro[6] and GnRH receptor antagonists that were both potent against human and rat receptors in vitro.[7]

The chemistry of azaindoles has been previously described.[8] A few classical methods, such as Fischer, Madelung, and Reissert procedures are the traditional methods used for the synthesis of most of the azaindoles, which suffer from harsh reaction conditions and modest yields.[9] Azaindoles have been synthesized from terminal alkynes using Sonogashira reaction,[10] from internal alkynes using heteroannulation[11] and by Heck reaction.[12] Recently, organometallic chemistry and other synthetic strategies have been used for the preparation of azaindole derivatives.[13]

The Pictet–Spengler reaction[14] is an important acid catalyzed transformation frequently used for the synthesis of tetrahydroisoquinolines or tetrahydro-β-carbolines from carbonyl compounds and phenyl ethylamines or tryptamines, respectively.[15] There is only one report each for the synthesis of 5 and 6-azaindoles by Pictet–Spengler reaction.[16,17]

We herein describe the formation of substituted-5-azaindoles using catalysts like TMSCl or TFA involving an amazing tandem one pot four steps reaction sequence and formation of tetrahydro-5-azaindoles in diastereoselective manner using glacial acetic acid as a catalyst during Pictet–Spengler condensation. No tandem reaction was observed during this condensation.

2. Results and discussions

Use of silica gel as a solid and mild acidic catalyst for various organic reactions is well reported.[18,19] In the present work silica gel has been used as a solid acidic catalyst for Michael addition reactions. Thus pyrroles **1** and **2** and nitro-olefins **4a**–**j** were loaded on silica gel and heated at 150 °C to furnish 2-alkyl pyrroles **5a**–**k** as major products in good yield. In some cases 2,5-dialkyl pyrroles **6a**–**c**, **6e**, and **6g** were obtained in minor amounts along with 2-alkyl pyrroles (Scheme 1, Table 1). The mono and dialkyl pyrroles were characterized by comparing the spectral data with the reported[20] values. *N*-Benzoyl pyrrole **3** failed to give the Michael adduct due to the withdrawing substituent at ring nitrogen.

Further, the nitro compounds **5a**, **5b**, **5c**, and **5e** were reduced using freshly prepared Raney Nickel in methanol to obtain amino compound **7**, **8**, **9**, and **10**, respectively, (Scheme 2).

Keeping in view tetrahydro-5-azaindoles as target molecules, Pictet–Spengler cyclization was attempted using conventional

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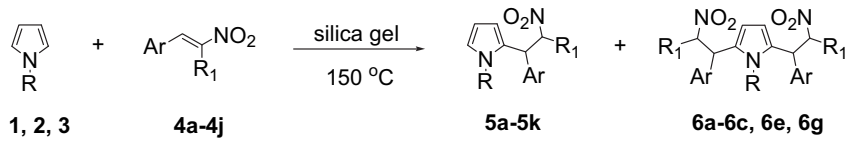


Scheme 1. Michael addition reaction of pyrrole **1** and **2** with nitro-olefins **4a**–**j**.

Table 1
Time and yield for the formation of Michael adducts **5** and **6**

Entry	R	Number (**4**–**6**)	Ar	R_1	Time (min)	Yield[a] (%)	
						5[b]	**6**[b]
1	H	**a**	4-Methoxyphenyl	H	4	85	9
2	H	**b**	Phenyl	H	1	90	6
3	H	**c**	3,4-Dimethoxyphenyl	H	4	84	10
4	H	**d**	3,4-Methylenedioxyphenyl	H	3	84	—
5	H	**e**	2-Furyl	H	1	83	10
6	H	**f**	4-Nitrophenyl	H	5	82	—
7	H	**g**	2-Thienyl	H	1	82	11
8	H	**h**	Phenyl	Me	5	81	—
9	H	**i**	3,4-Dimethoxyphenyl	Me	5	80	—
10	H	**j**	4-Nitrophenyl	Me	5	82	—
11	Me	**b**	Phenyl	H	3	83[c]	—

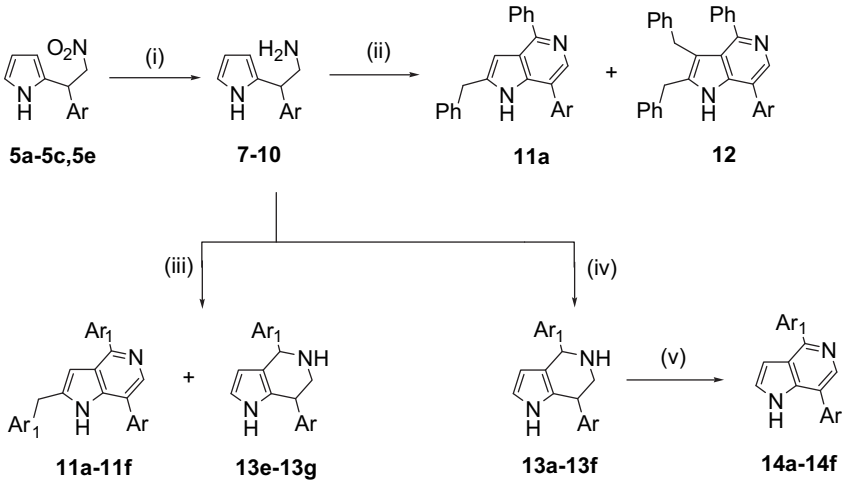
[a] Calculated according to the recovered starting electrophile.
[b] Products **5h**–**j** and **6a**–**c**, **6e**, and **6g** are mixture of diastereomers.
[c] Yield of Michael adduct **5k**

C_6H. DEPT spectrum showed the presence of one CH_2 group for compound **11a** and two for **12**.

The formation of **11a** and **12** can be explained by an amazing one pot four step reaction sequence involving first Pictet–Spengler cyclization followed by substitution at C_2 and C_3 with one or two molecules of benzaldehyde along with dehydration and subsequent dehydrogenation.

To achieve the planned target it was decided to check the reactions using TFA. Thus the reaction of amino compound **7** (0.002 mol) with benzaldehyde (0.004 mol) carried out in TFA for 15 h at room temperature furnished exclusively product **11a** in 61% yield. To confirm the generality of tandem four steps reaction sequence, Pictet–Spengler cyclization using amines **8**, **9**, and **10** with benzaldehyde was attempted to get trisubstituted-5-azaindoles **11b**, **11c**, and **11d**, respectively, as a single product (Scheme 2).

On the other hands, the reactions using substituted benzaldehydes with amino compound **10** led to different results in Pictet–Spengler cyclization. Trisubstituted-5-azaindole **11e** was



Scheme 2. Reagents and conditions: (i) Raney Nickel, H_2, MeOH; (ii) PhCHO, DCM, TMSCl, rt, 48 h.;(iii) Ar_1CHO, DCM, TFA, rt, 12–24 h; (iv) Ar_1CHO, DCM, AcOH (glacial), rt, 36–48 h; (v) Pd/C (5%), xylene, reflux. **5a**, **7**, **11a**, **13a**, **14a**: Ar=4-methoxyphenyl, Ar_1=phenyl; **5b**, **8**, **11b**: Ar, Ar_1=phenyl; **5c**, **9**, **11c**, **13b**, **14b**: Ar=3,4-dimethoxyphenyl, Ar_1=phenyl; **5e**, **10**, **11d**, **13c**, **14c**: Ar=2-furyl, Ar_1=phenyl; **11e**, **13d**, **14d**: Ar=2-furyl, Ar_1=4-methoxyphenyl; **11f**, **13e**, **14e**: Ar=2-furyl, Ar_1=4-chlorophenyl; **13f**, **13g**, (diastereomers), **14f**: Ar=2-furyl, Ar_1=4-nitrophenyl.

catalysts namely TMSCl and TFA. Initially, reaction of amine **7** with equal equivalents of benzaldehyde in the presence of TMSCl/TFA in dichloromethane was attempted. The reaction was very slow and gave minor amount of mixture of products along with starting amine. Thus excess of aldehydes was used for all the Pictet–Spengler cyclizations.

Treatment of amine **7** with excess of benzaldehyde in the presence of TMSCl furnished two products, one as yellow crystals, melting at 175–177 °C in 28% yield and the other as an oily liquid in 15% yield (Scheme 2). From the spectral data, the products were shown to be **11a** and **12**, respectively. Structure of **11a** was established by the presence of a singlet of two benzylic protons at 4.12 ppm and C_6H as a downfield singlet at 8.28 in ^1H NMR while structure **12** was confirmed by the presence of three singlets, two at 4.06 and 3.88 ppm, each of two benzylic protons and one at 8.25 of

obtained exclusively in the reaction of amine **10** with 4-methoxybenzaldehyde, while in the reaction with 4-chlorobenzaldehyde two products were formed; one was trisubstituted-5-azaindole **11f** and the other was one diastereomer of 4,7-disubstituted-4,5,6,7-tetrahydro-5-azaindole **13e**. Using 4-nitrobenzaldehyde, mixture of diastereomers of tetrahydro-5-azaindole **13f** and **13g** were obtained (Scheme 2). The separation of two diastereomers could be achieved successfully using column chromatography. In ^1H NMR, **13f** showed separate signals for three protons of C_6 and C_7 at δ 2.98 as a doublet, 3.25 as a multiplet and 4.19 as a broad singlet while in the spectrum of **13g** the same three protons resonate at δ 3.21–3.4 as a multiplet for two protons and 4.11 as a broad doublet for one proton.

By analyzing the results it was observed that in case of benzaldehyde and 4-methoxybenzaldehyde the reactions were fast to

furnish the trisubstituted-5-azaindoles by tandem four steps reaction sequence. While using 4-nitrobenzaldehyde due to the presence of electron-withdrawing group, reaction was slow and hence afforded only Pictet–Spengler cyclization furnishing two diastereomers of tetrahydro-5-azaindoles. In the reaction with 4-chlorobenzaldehyde mixed products were obtained due to lower withdrawing effect of chloro as compared nitro group.

Dehydrogenation of tetrahydro-5-azaindoles **13e** using 5% Pd/C gave product **14e** while that of the mixture of **13f** and **13g** gave 5-azaindoles **14f** along with some amount of starting **13f**. It was interesting to observe the ease of dehydrogenation of both the individual isomers. Dehydrogenation of **13f** furnished **14f** after 15 h along with 15% recovered starting while **13g** got dehydrogenated completely within 2 h. This indicated that **13g** reacted faster than **13f**, which suggested cis arrangement of the aryl and furyl groups at C_4 and C_7, respectively, in **13g** and *trans* in **13f** (Chart 1). In the later part X-ray analysis supported the trans stereochemistry.

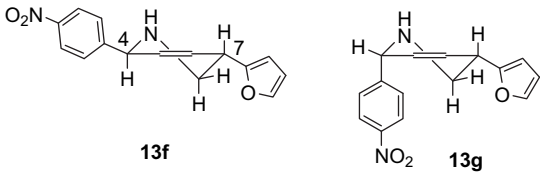


Chart 1.

The instability due to the cis arrangement of the bulky groups at C_4 and C_7 in **13g** forces the molecule to react faster to achieve the stable aromatic structure.

In case of Pictet–Spengler reaction with 4-chlorobenzaldehyde, the cis isomer initially formed might be undergoing further steps of substitution along with dehydration and subsequent dehydrogenation very fast to give **11f**. In contrast the isomer **13e**, not getting converted easily, must be having trans stereochemistry.

It was not possible to achieve the synthesis of targeted tetrahydro-5-azaindoles selectively using TMSCl or TFA in the Pictet–Spengler cyclizations, except in the reactions using benzaldehyde having electron-withdrawing substituents.

With the aim to get selectively tetrahydro-5-azaindoles, glacial acetic acid was used as a milder catalyst for this cyclization. As the reaction with 1 equiv of benzaldehyde was very slow, reaction of amine **7** with excess of benzaldehyde in the presence of glacial acetic acid was carried out, which furnished tetrahydro-5-azaindole **13a** as a single isomer in 68% yield, which was characterized by spectral data (Scheme 2). The formation of a diastereoselective product **13a** can be attributed to the mild acidic catalyst. In addition to the above product some amount of starting along with an unknown compound in very minor amount was seen on TLC. Further, dehydrogenation of **13a** by refluxing with 5% Pd/C in xylene furnished 4,7-disubstituted-5-azaindole **14a**.

Encouraged by the success in the diastereoselective cyclization reaction with glacial acetic acid, the substituents at C_4 and C_7 were changed to generalize the stereoselectivity in this reaction. Thus condensation of the amines **9** and **10** with benzaldehyde gave tetrahydro-5-azaindoles **13b** and **13c** as major products, respectively. Reactions of amine **10** with 4-methoxybenzaldehyde furnished **13d**, with 4-chlorobenzaldehyde furnished **13e**, and with 4-nitrobenzaldehyde furnished **13f** in diastereoselective manner (Scheme 2). The stereochemistry of **13b** was unambiguously investigated using single crystal X-ray analysis indicating trans geometry as *R*, *S* configuration at C_4 and C_7 (Fig. 1).

In the last step, refluxing 4,7-disubstituted-tetrahydro-5-azaindoles **13b–e** and **13f** with 5% Pd/C in xylene furnished 4,7-disubstituted-5-azaindoles **14b–e** and **14f**, respectively.

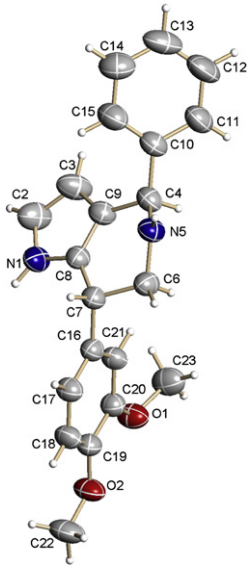


Fig. 1. ORTEP diagram of compound **13b** ellipsoid is drawn at 50% probability.

By analogy with **13b**, the diastereomer **13f** should have trans geometry, which also explains the slow rate of dehydrogenation of this compound. By comparing the ^{1}H NMR and dehydrogenation time (9–15 h), all products obtained in the reactions using glacial acetic acid were suggested to have trans geometry.

Recalling the reaction of amine **7** with benzaldehyde in the presence of glacial acetic acid, an unknown product was obtained, which was shown to be identical with the dehydrogenated product **14a**. During the Pictet–Spengler reaction of amine **10** with 4-methoxybenzaldehyde, aromatic product **14d** was detected in 10% yield along with 4,7-disubstituted-tetrahydro-5-azaindole **13d**. In all other similar reactions, TLC indicated the presence of minor amount of dehydrogenated product. As the cis isomer was shown to dehydrogenate faster, probably the initially formed small amount of cis isomer might be getting converted to the 4,7-disubstituted-5-azaindoles.

3. Conclusion

A diastereoselective method was established for the synthesis of 4,7-disubstituted-tetrahydro-5-azaindoles using glacial acetic acid as a mild catalyst during Pictet–Spengler reaction. The stereochemistry was shown to be trans using X-ray analysis. The method was used for synthesizing new 4,7-disubstituted-tetrahydro-5-azaindoles **13a–f**, which were dehydrogenated to 4,7-disubstituted-5-azaindoles **14a–f**. In a tandem four steps reaction sequence using stronger acid TFA, unreported 2,4,7-trisubstituted-5-azaindoles **11a–f** were synthesized in good yields.

4. Experimental section

4.1. General

Melting points recorded are uncorrected. All solvents were of reagent grade and, when necessary, were purified and dried by standard methods. Commercially available glacial acetic acid (from Merck) was used. Reactions and products were routinely monitored by thin layer chromatography (TLC) on silica gel (Kieselgel 60 F_{254}, Merck). Column chromatographic purifications were performed using 60–120 mesh silica gel. Visualization was made with UV light (254 and 365 nm) or with an iodine vapor. IR spectra were recorded on Shimadzu 8400 instrument. ^{1}H NMR spectra were recorded on (300 MHz) Varian Mercury instrument or Brucker AC 200

spectrometer (200 MHz) using TMS as an internal standard. ^{13}C NMR spectra were recorded on Varian Mercury instrument or Brucker ACF 200 spectrometer (75 and 50 MHz, respectively). ^{1}H NMR peaks expressed as s, br, d, dd, t, and m correspond to singlet, broad-singlet, doublet, doublet of doublet, triplet, and multiplet, respectively. Mass were recorded on Shimadzu QP 5050. Elemental analyses were recorded on Flash E. A. 1112 Thermo instrument.

4.2. General procedure for Michael addition of pyrrole on nitro-olefins

A mixture of pyrrole (**1**, **2** or **3**; 0.0024 mol) and nitro-olefin (**4a**–**i** or **4j**; 0.002 mol) was loaded on silica gel (60–120 mesh, 0.25 g) and heated on silica gel bath at 150 °C for 1–5 min. After the reaction was completed as judged by TLC, the same silica gel was loaded on a silica-gel column. Chromatographic separation using hexane/ethyl acetate furnished the products **5a**–**k** and **6a**, **6b**, **6d**, **6f**, and **6g**.

4.3. General procedure for Catalytic hydrogenation

The solution of 2-aryl-2-(2-pyrrolyl)-1-nitroethane (**5a**, **5b**, **5d** or **5e**, 0.002 mol) in methanol was taken in round bottom flask (10 ml) and Raney Nickel (1.5 g) was added to it. The reaction mixture was treated with hydrogen using balloon under hydrogen atmosphere and stirred for 2–12 h. The reaction was followed by TLC. After completion of reaction, mixture was filtered through Celite bed and filtrate was concentrated on rotary evaporator and washed with ether to remove soluble impurities. The semisolid product (**7**, **8**, **9** or **10**) was recrystallized from hot pet. ether.

4.3.1. 2-(4-Methoxyphenyl)-2-(1H-pyrrol-2-yl)ethanamine **7**. Yield 91% as a white crystals; mp 94–96 °C; [found: C, 72.41; H, 7.66; N, 13.32. $C_{13}H_{16}N_2O$ requires C, 72.19; H, 7.46; N, 12.95%]; IR (KBr) 3460, 3412, 3389 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 (2H, br, exchangeable with D_2O, NH_2), 3.18 (1H, dd, *J* 6.6, 12.1 Hz, C_1H), 3.3 (1H, dd, *J* 6.6, 12.1 Hz, C_1H), 3.78 (3H, s, OCH_3), 3.98 (1H, t, *J* 6.6 Hz, C_2H), 5.92 (1H, br, ArH), 6.13 (1H, d, *J* 2.5 Hz, ArH), 6.67 (1H, br, ArH), 6.84 (2H, d, *J* 8.5 Hz, ArH), 7.1 (2H, d, *J* 8.5 Hz, ArH), 8.84 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.3, 46.5, 55.3, 105.5, 108.0, 114.1 (2×ArC), 116.9, 129.0 (2×ArC), 132.7, 133.0, 158.5; MS *m*/*z* (%) 216 [M^+, 6], 199 (8), 186 (100), 171 (14).

4.3.2. 2-Phenyl-2-(1H-pyrrol-2-yl)ethanamine **8**. Yield 94% as a white crystals; mp 106–108 °C; [found: C, 77.18; H, 7.75; N, 15.26. $C_{12}H_{14}N_2$ requires C, 77.38; H, 7.58; N, 15.04%]; IR (KBr) 3427 (br), 3267 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (2H, br, exchangeable with D_2O, NH_2), 3.21 (1H, dd, *J* 6.3, 12.4 Hz, C_1H), 3.32 (1H, dd, *J* 6.3, 12.4 Hz, C_1H), 4.01 (1H, t, *J* 6.3 Hz, C_2H), 5.94 (1H, br, ArH), 6.13 (1H, d, *J* 2.8 Hz, ArH), 6.67 (1H, br, ArH), 7.13–7.35 (5H, m, ArH), 8.88 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.9, 47.0, 105.3, 107.8, 116.7, 126.7, 128.0 (2×ArC), 128.5 (2×ArC), 133.0, 141.5; MS *m*/*z* (%) 186 [M^+, 8], 156 (100), 141 (2), 91 (2.7).

4.3.3. 2-(3,4-Dimethoxyphenyl)-2-(1H-pyrrol-2-yl)ethanamine **9**. Yield 90% as a white crystals; mp 84–86 °C; [found: C, 68.07; H, 7.65; N, 11.59. $C_{14}H_{18}N_2O_2$ requires C, 68.27; H, 7.37; N, 11.37%]; IR (KBr) 3365 (br), 3269 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (2H, br, exchangeable with D_2O, NH_2), 3.2 (1H, dd, *J* 6.6, 12.1 Hz, C_1H), 3.33 (1H, dd, *J* 6.6, 12.1 Hz, C_1H), 3.82 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.94 (1H, t, *J* 6.3 Hz, C_2H), 5.94 (1H, br, ArH), 6.14 (1H, d, *J* 2.5 Hz, ArH), 6.65–6.83 (4H, m, ArH), 8.84 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.4, 46.9, 55.9 (2×OCH_3), 105.3, 107.9, 111.2, 111.3, 116.7, 120.1, 133.1, 133.8, 147.8, 148.9; MS *m*/*z* (%) 246 [M^+, 10], 231 (2), 216 (100), 200 (16), 185 (14).

4.3.4. 2-(2-Furyl)-2-(1H-pyrrol-2-yl)ethanamine **10**. Yield 89% as a white crystals; mp 59–61 °C; [found: C, 68.42; H, 6.52; N, 15.64. $C_{10}H_{12}N_2O$ requires C, 68.16; H, 6.86; N, 15.90%]; IR (KBr) 3340, 3286, 3243 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (2H, br, exchangeable with D_2O, NH_2), 3.21 (2H, br, C_1H), 4.08 (1H, br, C_2H), 5.98 (1H, br, ArH), 6.04(1H, br, ArH), 6.12 (1H, br, ArH), 6.29 (1H, br, ArH), 6.68 (1H, br, ArH), 7.34 (1H, br, ArH), 8.99 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.5, 45.7, 105.7, 106.5, 107.9, 110.1, 116.9, 130.5, 141.5, 154.9; MS *m*/*z* (%) 176 [M^+, 14], 146 (100), 130 (12), 117 (95).

4.4. General procedure for Pictet–Spengler reaction

A solution of amino compound (**7**, **8**, **9** or **10**; 0.002 mol) in dichloromethane was treated at room temperature with aromatic aldehyde (0.004 mol or 0.006 mol in case of TMSCl). The solution was cooled and trimethyl silyl chloride or trifluoroacetic acid or glacial acetic acid (0.004 mol) was slowly added over 15 min to it. The reaction mixture was stirred at room temperature for 48 h in case of TMSCl or for 12–24 h using TFA or for 36–48 h using glacial acetic acid. The reaction mixture was diluted with dichloromethane. Sodium hydroxide (10%) (for the reaction in TMSCl) or saturated aqueous sodium hydrogen carbonate (for the reactions in other acids) was added and the organic phase was separated. The aqueous phase was extracted with dichloromethane (2×50 ml); the organic extracts were combined and dried over sodium sulfate. The crude product obtained was chromatographed on silica gel using pet. ether and ethyl acetate as an eluent yielding the pure products.

4.4.1. 2-Benzyl-4-phenyl-7-(4-methoxyphenyl)-1H-pyrrolo[3,2-c] pyridine ***11a***. Yield 61% (using TFA, stirring time 15 h), 28% (using TMSCl, stirring time 48 h) as a yellow solid; mp 175–177 °C; [found: C, 82.84; H, 5.91; N, 6.89. $C_{27}H_{22}N_2O$ requires C, 83.05; H, 5.68; N, 7.17%]; R_f (30% EtOAc/hexane) 0.33; IR (KBr) 3367 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.81 (3H, s, OCH_3), 4.12 (2H, s, CH_2), 6.65 (1H, s, ArH), 6.97 (2H, d, *J* 7.9 Hz, ArH), 7.15–7.29 (5H, m, ArH), 7.4 (1H, d, *J* 6.3 Hz, ArH), 7.46–7.48 (4H, m, ArH), 7.96 (2H, d, *J* 6.6 Hz, ArH), 8.28 (1H, s, ArH), 8.67 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.5, 55.3, 101.6, 114.6 (2×ArC), 119.5, 122.9, 126.8, 127.7, 128.4 (3×ArC), 128.5 (2×ArC), 128.6 (3×ArC), 128.7 (2×ArC), 129.2 (2×ArC), 137.6, 138.5, 139.3, 140.2, 149.2, 159.3; MS *m*/*z* (%) 390 [M^+, 100], 375 (5), 359 (1), 313 (7), 299 (3.5), 281 (2.5), 91 (18), 77 (6). DEPT (75 MHz, $CDCl_3$) showed the presence of one CH_2 group and one CH_3 group.

4.4.2. 2-Benzyl-4,7-diphenyl-1H-pyrrolo[3,2-c]pyridine ***11b***. Yield 69% (using TFA, stirring time 12 h) as a white crystals; mp 170–172 °C; [found: C, 86.41; H, 5.39; N, 8.03. $C_{26}H_{20}N_2$ requires C, 86.64; H, 5.59; N, 7.77%]; R_f (30% EtOAc/hexane) 0.41; IR (KBr) 3444 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.06 (2H, s, CH_2), 6.61 (1H,s, ArH), 6.98–7.29 (6H, m, ArH), 7.32–7.49 (5H, m, ArH), 7.52 (2H, d, *J* 7.2 Hz, ArH), 7.91 (2H, d, *J* 7.2 Hz, ArH), 8.27 (1H, s, ArH), 9.13 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.4, 101.5, 119.7, 122.9, 126.7, 127.8, 128.1 (2×ArC), 128.3 (2×ArC), 128.4 (2×ArC), 128.5 (2×ArC), 128.6 (3×ArC), 129.1 (2×ArC), 135.7, 137.6, 138.9, 139.1, 139.4, 140.0, 149.9; MS *m*/*z* (%) 360 [M^+, 100], 283 (6.7), 269 (4.4), 205 (2.2), 113 (2.2), 91 (3.3), 77 (2.2).

4.4.3. 2-Benzyl-4-phenyl-7-(3,4-dimethoxyphenyl)-1H-pyrrolo-[3,2-c]pyridine ***11c***. Yield 70% (using TFA, stirring time 15 h) as a white crystals; mp 185–187 °C; [found: C, 80.23; H, 5.59; N, 6.91.

$C_{28}H_{24}N_2O_2$ requires C, 79.98; H, 5.75; N, 6.66%]; R_f (30% EtOAc/hexane) 0.29; IR (KBr) 3348 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.82 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.17 (2H, s, CH_2), 6.69 (1H, s, ArH), 6.96–7.01 (2H, m, ArH), 7.12 (1H, d, *J* 8.3 Hz, ArH), 7.19–7.36 (5H, m, ArH), 7.42 (1H, t, *J* 7.2 Hz, ArH), 7.5 (2H, t, *J* 7.4 Hz, ArH), 7.99 (2H, d, *J* 7.4 Hz, ArH), 8.32 (1H, br, exchangeable with D_2O, NH of pyrrole ring), 8.35 (1H, s, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.5, 55.8 (2×OCH_3), 101.3, 111.1, 111.6, 119.6, 120.4, 122.8, 126.7, 128.23, 128.26, 128.33 (2×ArC), 128.49 (2×ArC), 128.5 (2×ArC), 128.6 (2×ArC), 137.7, 138.8, 139.2, 139.6, 139.9, 148.6, 149.3, 149.6; MS *m*/*z* (%) 420 [M^+, 100], 419 (54), 403 (14), 389 (5), 343 (4), 91 (11), 77 (2).

4.4.4. 2-Benzyl-4-phenyl-7-(2-furyl)-1H-pyrrolo[3,2-c]pyridine ***11d***. Yield 68% (using TFA, stirring time 16 h) as oily liquid; [found: C, 82.02; H, 5.43; N, 7.69. $C_{24}H_{18}N_2O$ requires C, 82.26; H, 5.18; N, 7.99%]; R_f (30% EtOAc/hexane) 0.40; IR (KBr) 3462 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.23 (2H, s, CH_2), 6.58 (1H, m, ArH), 6.68 (1H, br, ArH), 6.84 (1H, d, *J* 3.6 Hz, ArH), 7.23–7.4 (5H, m, ArH), 7.44 (1H, d, *J* 7.2 Hz, ArH), 7.52 (2H, t, *J* 7.4 Hz, ArH), 7.57 (1H, br, ArH), 8.01 (2H, d, *J* 7.2 Hz, ArH), 8.65 (1H, s, ArH), 9.15 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.4, 101.0, 105.4, 109.5, 111.6, 123.2, 126.7, 128.1, 128.3 (2×ArC), 128.4 (2×ArC), 128.5 (2×ArC), 128.6 (2×ArC), 136.3, 136.4, 137.6, 139.7, 139.9, 141.9, 149.9, 151.4; MS *m*/*z* (%) 349 [M^+-1, 100], 319 (14), 273 (12), 259 (9), 91 (20), 77 (12).

4.4.5. 2-(4-Methoxybenzyl)-4-(4-methoxyphenyl)-7-(2-furyl)-1H-pyrrolo[3,2-c]pyridine ***11e***. Yield 61% (using TFA, stirring time 20 h) as oily liquid; [found: C, 76.31; H, 5.57; N, 7.09. $C_{26}H_{22}N_2O_3$ requires C, 76.08; H, 5.40; N, 6.82%]; R_f (30% EtOAc/hexane) 0.28; IR (KBr) 3456 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.82 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 4.16 (2H, s, CH_2), 6.56 (1H, m, ArH), 6.63 (1H, br, ArH), 6.81 (1H, d, *J* 3.6 Hz, ArH), 6.88 (2H, d, *J* 8.5 Hz, ArH), 7.05 (2H, d, *J* 8.8 Hz, ArH), 7.19 (2H, d, *J* 8.5 Hz, ArH), 7.57 (1H, br, ArH), 7.95 (2H, d, *J* 8.8 Hz, ArH), 8.61 (1H, s, ArH), 9.1 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.7, 55.2, 55.3, 100.8, 105.1, 109.0, 111.6, 113.8 (2×ArC), 114.0 (2×ArC), 122.8, 129.5 (2×ArC), 129.7 (2×ArC), 132.6, 136.3, 136.4 (2×ArC), 139.9, 141.8, 149.7, 151.6, 158.2, 159.6; MS *m*/*z* (%) 410 [M^+, 100], 395 (16), 381 (2.1), 303 (3), 108 (6.3), 91 (2.1), 77 (4.2).

4.4.6. 2-(4-Chlorobenzyl)-4-(4-chlorophenyl)-7-(2-furyl)-1H-pyrrolo[3,2-c]pyridine ***11f***. Yield 31% (using TFA, stirring time 24 h) as a yellowish solid; R_f (30% EtOAc/hexane) 0.36; IR (KBr) 3363 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (2H, s, CH_2), 6.56 (1H, br, ArH), 6.81 (1H, d, *J* 3.0 Hz, ArH), 7.13–7.42 (6H, m, ArH), 7.46 (1H, d, *J* 6.9 Hz, ArH), 7.58 (1H, br, ArH), 7.9 (2H, d, *J* 6.9 Hz, ArH), 8.61 (1H, s, ArH), 9.31 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$/DMSO-d_6): δ 33.9, 100.7, 105.9, 109.6, 110.8, 121.8, 126.9 (2×ArC), 127.5 (2×ArC), 128.9 (2×ArC), 129.2 (2×ArC), 130.9, 132.9, 134.5, 135.2, 136.4, 137.3, 140.7, 141.6, 147.8, 149.1. Additional signals of **13e** were also seen in the spectrum.

4.4.7. 2,3-Dibenzyl-4-phenyl-7-(4-methoxyphenyl)-1H-pyrrolo-[3,2-c]pyridine ***12***. Yield 15% (using TMSCl, stirring time 48 h) as oily liquid; [found: C, 85.19; H, 6.09; N, 5.61. $C_{34}H_{28}N_2O$ requires C, 84.97; H, 5.87; N, 5.83%]; R_f (30% EtOAc/hexane) 0.24; IR (KBr) 3450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.84 (3H, s, OCH_3), 3.88 (2H, s, CH_2), 4.06 (2H, s, CH_2), 6.66 (2H, br, ArH), 6.96–7.13 (7H, m, ArH), 7.18–7.3 (6H, m, ArH), 7.34 (2H, t, *J* 6.6 Hz, ArH), 7.49 (2H, d, *J* 8.8 Hz, ArH), 8.25 (1H, s, ArH), 8.33 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.4, 32.4, 55.4, 111.4, 114.8 (2×ArC), 119.0, 122.2, 125.3, 126.8, 127.5 (2×ArC), 127.6, 127.7 (2×ArC), 127.8 (2×ArC), 128.0, 128.4 (2×ArC), 128.8 (2×ArC), 129.1 (2×ArC), 129.2 (2×ArC), 136.2, 137.6, 138.5, 138.8, 140.5, 140.6, 152.2, 159.3; MS *m*/*z* (%) 480 [M^+, 100], 448 (1), 403 (6.6), 389 (5.5), 374 (2.2), 311 (2.4), 297 (1), 91 (5.5), 77 (3.3). DEPT (75 MHz, $CDCl_3$) showed the presence of two CH_2 groups and one CH_3 group.

4.4.8. 4-Phenyl-7-(4-methoxyphenyl)-4,5,6,7-tetrahydro-1H-pyrrolo [3,2-c]pyridine ***13a***. Yield 68% (using AcOH, stirring time 36 h) as a white solid; mp 152–154 °C; [found: 78.71; H, 6.84; N, 8.96. $C_{20}H_{20}N_2O$ requires C, 78.92; H, 6.62; N, 9.20%]; R_f (50% EtOAc/hexane) 0.28; IR (KBr) 3398 (br) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.7 (1H, br, exchangeable with D_2O, NH), 2.94 (1H, dd, *J* 9.4, 12.3 Hz, C_6H), 3.39 (1H, dd, *J* 5.2, 12.3 Hz, C_6H), 3.78 (3H, s, OCH_3), 4.1 (1H, t, *J* 5.8 Hz, C_7H), 5.11 (1H, d, *J* 1.4 Hz, C_4H), 5.74 (1H, t, *J* 2.3 Hz, ArH), 6.55 (1H, t, *J* 2.6 Hz, ArH), 6.84 (2H, d, *J* 8.5 Hz, ArH), 7.08 (2H, d, *J* 8.5 Hz, ArH), 7.21–7.44 (5H, m, ArH), 7.89 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.3, 52.7, 55.3, 58.8, 105.8, 114.0 (2×ArC), 116.5, 120.2, 127.4, 128.2 (2×ArC), 128.3 (2×ArC), 128.7, 129.3 (2×ArC), 133.9, 144.0, 158.6; MS *m*/*z* (%) 304 [M^+, 2.2], 275 (100), 260 (13.2), 244 (30), 198 (16.3), 91 (8.8), 77 (13.2).

4.4.9. 4-Phenyl-7-(3,4-dimethoxyphenyl)-4,5,6,7-tetrahydro-1H-pyrrolo[3,2-c]pyridine ***13b***. Yield 66% (using AcOH, stirring time 36 h) as a white solid; mp 169–171 °C; [found: C, 75.69; H, 6.85; N, 8.67. $C_{21}H_{22}N_2O_2$ requires C, 75.42; H, 6.63; N, 8.38%]; R_f (50% EtOAc/hexane) 0.25; IR (KBr): 3553, 3277 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$/DMSO-d_6) δ 3.04 (1H, t, *J* 11.7 Hz, C_6H), 3.49 (1H, dd, *J* 4.7, 12.0 Hz, C_6H), 3.79 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 4.27 (1H, br, C_7H), 5.35 (1H, br, C_4H), 5.67 (1H, br, exchangeable with D_2O, NH), 6.61 (1H, s, ArH), 6.72 (2H, m, ArH), 6.82 (1H, d, *J* 7.9 Hz, ArH), 7.25–7.39 (3H, m, ArH), 7.44 (2H, t, *J* 6.5 Hz, ArH), 7.94 (1H, d, *J* 7.3 Hz, ArH), 9.51 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$/DMSO-d_6) δ 39.4, 50.4, 55.0, 55.1, 57.6, 104.5, 110.6, 110.7, 116.6, 117.2, 119.8, 126.8, 127.0, 127.5, 128.1, 128.6, 130.3, 133.3, 140.9, 147.2, 148.2; MS *m*/*z* (%) 333 [M^+-1, 2], 305 (34), 290 (6), 274 (22), 259 (3), 243 (2), 77 (100).

4.4.10. 4-Phenyl-7-(2-furyl)-4,5,6,7-tetrahydro-1H-pyrrolo[3,2-c] pyridine ***13c***. Yield 60% (using AcOH, stirring time 36 h) as a white solid; mp 129–131 °C; [found: C, 77.54; H, 6.36; N, 10.89. $C_{17}H_{16}N_2O$ requires C, 77.25; H, 6.10; N, 10.60%]; R_f (50% EtOAc/hexane) 0.48; IR (KBr): 3356, 3259 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.0 (1H, br, exchangeable with D_2O, NH), 3.19 (1H, dd, *J* 8.2, 12.3 Hz, C_6H), 3.49 (1H, dd, *J* 5.3, 12.3 Hz, C_6H), 4.24 (1H, t, *J* 6.5 Hz, C_7H), 5.07 (1H, d, *J* 1.5 Hz, C_4H), 5.79 (1H, t, *J* 2.6 Hz, ArH), 6.08 (1H, d, *J* 3.3 Hz, ArH), 6.34 (1H, m, ArH), 6.61 (1H, t, *J* 2.3 Hz, ArH), 7.25–7.41 (6H, m, ArH), 8.32 (1H, br, exchangeable with D_2O, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.0, 47.8, 58.3, 105.6, 106.1, 110.2, 116.6, 119.6, 125.8, 127.3, 128.2 (2×ArC), 128.3 (2×ArC), 141.7, 144.0, 155.1; MS *m*/*z* (%) 235 [M^+-29, 100%], 218 (7.6), 206 (65), 191 (7.8), 77 (28), 51 (33).

4.4.11. 4-(4-Methoxyphenyl)-7-(2-furyl)-4,5,6,7-tetrahydro-1H-pyrrolo[3,2-c]pyridine ***13d***. Yield 61% (using AcOH, stirring time 48 h) as a white solid; mp 146–148 °C; [found: C, 73.19; H, 6.38; N, 9.22. $C_{18}H_{18}N_2O_2$ requires C, 73.45; H, 6.16; N, 9.52%]; R_f (50% EtOAc/hexane) 0.29; IR (KBr) 3362, 3248 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 1.87 (1H, br, exchangeable with D_2O, NH), 2.90 (1H, dd, *J* 8.2, 12.3 Hz, C_6H), 3.26 (1H, dd, *J* 5.3, 12.3 Hz, C_6H), 3.71 (3H, s, OCH_3), 4.16 (1H, br, C_7H), 4.84 (1H, s, C_4H), 5.46 (1H, s, ArH), 6.08 (1H, d, *J* 2.9 Hz, ArH), 6.38 (1H, m, ArH), 6.50 (1H, s, ArH), 6.83 (2H, d, *J* 8.5 Hz, ArH), 7.21 (2H, d, *J* 8.5 Hz, ArH), 7.56 (1H, d, *J* 0.9 Hz, ArH), 10.38 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, DMSO-d_6) δ 34.4, 48.0, 55.0, 56.8, 104.8, 105.9, 110.3, 113.2

(2×ArC), 116.6, 119.5, 124.8, 129.2 (2×ArC), 136.6, 141.7, 155.6, 158.2; MS *m*/*z* (%) 295 [M^++1, 12], 283 (14), 207 (20), 110 (16), 44 (100).

4.4.12. 4-(4-Chlorophenyl)-7-(2-furyl)-4,5,6,7-tetrahydro-1H-pyrrolo[3,2-c]pyridine ***13e***. Yield 59% (using AcOH, stirring time 48 h), 33% (using TFA, stirring time 24 h) as a white solid; mp 164–166 °C; [found: C, 68.09; H, 4.89; N, 9.11. $C_{17}H_{15}ClN_2O$: requires C, 68.34; H, 5.06; N, 9.38%]; R_f (50% EtOAc/hexane) 0.58; IR (KBr) 3362, 3248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.93 (1H, br, exchangeable with D_2O, NH), 3.17 (1H, dd, *J* 8.3, 12.4 Hz, C_6H), 3.45 (1H, dd, *J* 5.2, 12.4 Hz, C_6H), 4.23 (1H, t, *J* 7.15 Hz, C_7H), 5.02 (1H, d, *J* 1.7 Hz, C_4H), 5.73 (1H, t, *J* 2.5 Hz, ArH), 6.06 (1H, d, *J* 3.3 Hz, ArH), 6.32 (1H, m, ArH), 6.62 (1H, t, *J* 2.8 Hz, ArH), 7.28–7.34 (4H, m, ArH), 7.37 (1H, m, ArH), 8.22 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.9, 47.7, 57.6, 105.7, 106.0, 110.2, 116.8, 119.3, 125.9, 128.4 (2×ArC), 129.6 (2×ArC), 132.9, 141.8, 142.6, 154.9; MS *m*/*z* (%) 269 [M^+−29, 100], 240 (30.8), 234 (22), 205 (35.4), 151 (6.6), 51 (30.8).

4.4.13. 4-(4-Nitrophenyl)-7-(2-furyl)-4,5,6,7-tetrahydro-1H-pyrrolo [3,2-c]pyridine ***13f***. Yield 52% (using AcOH, stirring time 48 h), 34% (using TFA, stirring time 24 h) as a yellow crystals; mp 163–164 °C; [found: C, 65.79; H, 5.15; N, 13.36. $C_{17}H_{15}N_3O_3$ requires C, 66.01; H, 4.89; N, 13.58%]; R_f (30% EtOAc/hexane) 0.29; IR (KBr) 3351, 3219, 1518, 1344 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 2.50 (1H, br, exchangeable with D_2O, NH), 2.98 (1H, br d, *J* 6.9 Hz, C_6H), 3.25 (1H, m, with DMSO, C_6H), 4.19 (1H, br, C_7H), 5.09 (1H, br, C_4H), 5.46 (1H, br, ArH), 6.09 (1H, br, ArH), 6.38 (1H, br, ArH), 6.53 (1H, br, ArH), 7.55 (1H, br, ArH), 7.60 (2H, d, *J* 7.7 Hz, ArH), 8.19 (2H, d, *J* 7.2 Hz, ArH), 10.45 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, DMSO-d_6): δ 34.3, 47.5, 56.4, 104.5, 105.8, 110.1, 116.7, 118.1, 122.9 (2×ArC), 124.9, 128.9 (2×ArC), 141.4, 146.1, 152.9, 155.3; MS *m*/*z* (%) 280 [M^+−29, 100], 279 (8), 263 (8), 233 (23), 217 (2.5), 51 (2.2).

4.4.14. 4-(4-Nitrophenyl)-7-(2-furyl)-4,5,6,7-tetrahydro-1H-pyr-rolo[3,2-c]pyridine ***13g***. Yield 24% (using TFA, stirring time 24 h) as a oily liquid; [found: C, 66.32; H, 4.59; N, 13.42. $C_{17}H_{15}N_3O_3$ requires C, 66.01; H, 4.89; N, 13.58%]; R_f (30% EtOAc/hexane) 0.22; IR (KBr) 3416 (br), 1518, 1346 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.69 (1H, br, exchangeable with D_2O, NH), 3.21–3.4 (2H, m, C_6H), 4.11 (1H, br d, *J* 4.7 Hz, C_7H), 5.15 (1H, br, C_4H), 5.74 (1H, t, *J* 2.5 Hz, ArH), 6.05 (1H, d, *J* 3.0 Hz, ArH), 6.29 (1H, t, *J* 1.7 Hz, ArH), 6.68 (1H, t, *J* 2.5 Hz, ArH), 7.34 (1H, br, ArH), 7.52 (2H, d, *J* 8.5 Hz, ArH), 8.14 (2H, d, *J* 8.5 Hz, ArH), 8.32 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.1, 46.2, 56.8, 105.7, 106.3, 110.2, 117.3, 117.7, 123.6 (2×ArC), 125.6, 129.2 (2×ArC), 141.8, 147.1, 150.9, 155.2; MS *m*/*z* (%) 281 [M^+−28, 30], 280 (100), 263 (14), 233 (24), 217 (4), 77 (5), 51 (2).

4.5. General procedure for dehydrogenation of disubstituted-tetrahydro-5-azaindoles

A mixture of tetrahydro-5-azaindole (**13a**–**f** or **13g**; 0.10 g), 5% Pd/C (50 mg) and dry xylene (5 ml) was refluxed for 2–15 h. The reaction mixture was cooled and ethyl acetate (10 ml) was added to it. The catalyst was filtered off through Celite and the filtrate was concentrated by rotary evaporator. The crude product obtained was chromatographed on neutral alumina using pet. ether and ethyl acetate as an eluent yielding disubstituted-5-azaindole.

4.5.1. 4-Phenyl-7-(4-methoxyphenyl)-1H-pyrrolo[3,2-c]pyridine ***14a***. Yield 81% as a white solid; mp 195–197 °C; [found: C, 79.72; H, 5.16; N, 9.08. $C_{20}H_{16}N_2O$ requires C, 79.98; H, 5.37; N, 9.33%]; R_f (30% EtOAc/hexane) 0.22; IR (KBr) 3201 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$/DMSO-d_6) δ 3.22 (3H, s, OCH_3), 6.27 (1H, d, *J* 4.0 Hz, ArH), 6.41 (2H, d, *J* 10.0 Hz, ArH), 6.67–6.95 (4H, m, ArH), 6.98 (2H, t, *J* 8.0 Hz, ArH), 7.42 (2H, d, *J* 8.0 Hz, ArH), 7.66 (1H, s, ArH), 10.07 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (50 MHz, $CDCl_3$/DMSO-d_6) δ 55.0, 102.2, 114.3 (2×ArC), 119.9, 122.2, 126.4, 127.9, 128.1, 128.2 (2×ArC), 128.4 (2×ArC), 129.3 (2×ArC), 138.4, 138.7, 139.6, 150.1, 159.1; MS *m*/*z* (%) 300 [M^+, 100%], 285 (39), 269 (2), 190 (1), 114 (23), 77 (4).

4.5.2. 4-Phenyl-7-(3,4-dimethoxyphenyl)-1H-pyrrolo[3,2-c]pyridine ***14b***. Yield 68% as a white solid; mp 163–165 °C; [found: C, 76.09; H, 5.71; N, 8.21. $C_{21}H_{18}N_2O_2$ requires C, 76.34; H, 5.49; N, 8.48%]; R_f (30% EtOAc/hexane) 0.18; IR (KBr) 3335 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.91 (6H, s, 2×OCH_3), 6.91 (1H, d, *J* 2.2 Hz, ArH), 6.98 (1H, d, *J* 8.3 Hz, ArH), 7.12 (1H, s, ArH), 7.18 (1H, d, *J* 8.3 Hz, ArH), 7.28 (1H, br, ArH), 7.38–7.46 (1H, m, ArH), 7.53 (2H, t, *J* 7.4 Hz, ArH), 8.0 (2H, d, *J* 7.7 Hz, ArH), 8.37 (1H, s, ArH), 9.1 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.8 (2×ArC), 103.0, 111.3, 111.5, 120.3, 120.5, 122.3, 126.3, 127.8, 128.1, 128.4 (2×ArC), 128.6 (2×ArC), 138.5, 138.8, 139.2, 148.7, 149.2, 150.4; MS *m*/*z* (%) 330 [M^+, 100], 315 (22), 297 (2), 194 (4), 109 (14).

4.5.3. 4-Phenyl-7-(2-furyl)-1H-pyrrolo[3,2-c]pyridine ***14c***. Yield 63% as a white solid; mp 162–164 °C; [found: C, 78.17; H, 4.89; N, 10.97. $C_{17}H_{12}N_2O$ requires C, 78.44; H, 4.65; N, 10.76%]; R_f (30% EtOAc/hexane) 0.37; IR (KBr) 3222 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$/DMSO-d_6) δ 6.33 (1H, t, *J* 2.0 Hz, ArH), 6.56 (1H, d, *J* 2.0 Hz, ArH), 6.72 (1H, d, *J* 4.0 Hz, ArH), 7.15–7.36 (4H, m, ArH), 7.39 (1H, d, *J* 10.0 Hz, ArH), 7.72 (2H, d, *J* 8.0 Hz, ArH), 8.4 (1H, s, ArH), 10.83 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (50 MHz, $CDCl_3$/DMSO-d_6) δ 102.2, 106.7, 110.5, 111.9, 123.0, 127.5, 128.6 (2×ArC), 128.7 (2×ArC), 135.7, 136.3, 139.9, 142.6 (2×ArC), 150.5, 150.6; MS *m*/*z* (%) 260 [M^+, 100], 231 (34), 204 (10), 76 (8).

4.5.4. 4-(4-Methoxyphenyl)-7-(2-furyl)-1H-pyrrolo[3,2-c]pyridi-ne ***14d***. Yield 65% as a white solid; mp 170–171 °C; [found: C, 74.24; H, 5.11; N, 9.39. $C_{18}H_{14}N_2O_2$ requires C, 74.47; H, 4.86; N, 9.65%]; R_f (30% EtOAc/hexane) 0.23; IR (KBr) 3215 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.87 (3H, s, OCH_3), 6.56 (1H, br, ArH), 6.88 (2H, br, ArH), 7.03 (2H, d, *J* 8.5 Hz, ArH), 7.36 (1H, br, ArH), 7.59 (1H, br, ArH), 7.95 (2H, d, *J* 8.5 Hz, ArH), 8.64 (1H, s, ArH), 9.77 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.3, 102.8, 105.4, 109.7, 111.7, 113.8 (2×ArC), 122.2, 125.8, 129.9 (2×ArC), 132.2, 135.9, 136.2, 142.0, 150.5, 151.3, 159.9; MS *m*/*z* (%) 290 [M^+, 100], 275 (32), 191 (12), 115 (9), 109 (16).

4.5.5. 4-(4-Chlorophenyl)-7-(2-furyl)-1H-pyrrolo[3,2-c]pyridine ***14e***. Yield 55% as a white solid; mp 180–182 °C; [found: C, 69.51; H, 3.99; N, 9.78. $C_{17}H_{11}ClN_2O$ requires C, 69.28; H, 3.76; N, 9.50%]; R_f (30% EtOAc/hexane) 0.33; IR (KBr) 3257 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$/DMSO-d_6) δ 6.59 (1H, t, *J* 1.7 Hz, ArH), 6.82 (1H, br, ArH), 7.02 (1H, d, *J* 3.0 Hz, ArH), 7.37–7.43 (1H, m, ArH), 7.5 (2H, t, *J* 8.0 Hz, ArH), 7.68 (1H, br, ArH), 7.98 (2H, d, *J* 8.0 Hz, ArH), 8.66 (1H, s, ArH), 11.23 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, $CDCl_3$/DMSO-d_6) δ 101.4, 106.3, 109.8, 111.4, 122.3, 126.9, 127.8, 127.9 (2×ArC), 128.1 (2×ArC), 134.9, 136.0 (2×ArC), 139.6, 142.0, 149.8; MS *m*/*z* (%) 294 [M^+, 10], 293 (6), 260 (100), 192 (8), 116 (98), 76 (58).

4.5.6. 4-(4-Nitrophenyl)-7-(2-furyl)-1H-pyrrolo[3,2-c]pyridine ***14f***. Yield 46% as a yellow solid; mp 155–157 °C; [found: C, 67.11; H, 3.42; N, 14.03. $C_{17}H_{11}N_3O_3$ requires C, 66.88; H, 3.63; N, 13.76%]; R_f (30% EtOAc/hexane) 0.25; IR (KBr) 3217, 1518, 1377 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 6.77 (1H, t, *J* 3.3 Hz, ArH), 6.98 (1H, br, ArH), 7.31 (1H, d, *J* 3.8 Hz, ArH), 7.69 (1H, d, *J* 2.8 Hz, ArH), 7.94 (1H, br, ArH),

8.32 (2H, d, *J* 8.8 Hz, ArH), 8.4 (2H, d, *J* 8.8 Hz, ArH), 8.78 (1H, s, ArH), 11.81 (1H, br, exchangeable with D_2O, NH of pyrrole ring); ^{13}C NMR (75 MHz, DMSO-d_6) δ 101.4, 108.2, 111.1, 112.4, 123.1, 123.9 (2×ArC), 129.4, 129.6 (2×ArC), 135.1, 136.5, 143.8, 146.0, 146.8, 147.1, 149.4; MS *m*/*z* (%) 305 [M^+, 16], 304 (4), 275 (100), 259 (30).

5. Crystallography

Crystallographic data in this paper have been deposited with the Cambridge Crystallographic Data Centre. Deposition number is CCDC 796855 for **13b**. Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +336033 1223 44 or e-mail: deposit@ccdc.cam.ac.uk).

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Supplementary data

Copies of ^1H, ^{13}C NMR spectra for new compounds and details of X-ray analysis of compound **13b** are associated with this article as supplementary data. Supplementary data associated with this article can be found in online version, at doi:10.1016/j.tet.2010.12.003. These data include MOL files and InChIKeys of the most important compounds described in this article.

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